POTTER

Molecular Rearrangements in the Camphor Series. Structure of the Amino Acids

Chemistry

Ph. D.

1913

UNIV. OF
ILLINOIS
LIBRARY

THE UNIVERSITY
OF ILLINOIS
LIBRARY
1913
P85

Digitized by the Internet Archive
in 2013

http://archive.org/details/molecularrearran00pott

MOLECULAR REARRANGEMENTS IN THE CAMPHOR SERIES. STRUCTURE OF THE AMINO ACIDS

BY

RALPH SYDNEY POTTER

A. B. Lake Forest College,
1909.
M. S. University of Illinois,
1911.

THESIS

Submitted in Partial Fulfillment of the Requirements for the

Degree of

DOCTOR OF PHILOSOPHY

IN CHEMISTRY

IN

THE GRADUATE SCHOOL

OF THE

UNIVERSITY OF ILLINOIS

1913

1913
P35

UNIVERSITY OF ILLINOIS

THE GRADUATE SCHOOL

May 13, 1913 190

I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY SUPERVISION BY

Ralph Sydney Potter

ENTITLED Molecular Rearrangements in the Camphor Series.

Structure of the Amino Acids.

BE ACCEPTED AS FULFILLING THIS PART OF THE REQUIREMENTS FOR THE

DEGREE OF Doctor of Philosophy

W. A. Noyes
In Charge of Major Work

W. A. Noyes
Head of Department

Recommendation concurred in:

Otto Rahn
D. A. MacInnes.
Geo. D. Beal
C. G. Derick

Committee on Final Examination

247437

UIUC

The following work was undertaken in the Chemical Laboratory of the University of Illinois early in the winter of 1912 - 1913, at the suggestion of Professor W. A. Noyes.

The writer takes this opportunity to express his most sincere thanks and appreciation to Professor Noyes, not only for the very valuable help he has given in connection with the present investigation, but also for the opportunity of learning the view point of a sincere teacher and a true scientist, such as he is.

Thanks are also due Mr. L. F. Nickell for the use of some unpublished data of his.

TABLE OF CONTENTS.

PART I. HISTORICAL

1. Concerning the work previously done on the compounds involved 1

2. The structure of the amino acids 15

PART II. THEORETICAL

1. Conditions for inner salt formation in amino acids 20

2. No inversion in the preparation of aminocamphonanic acid from α-camphoramidic acid 41

PART III. EXPERIMENTAL 46

PART I.

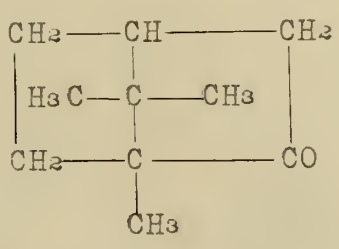
HISTORICAL.

PART I.

HISTORICAL.

1. CONCERNING THE WORK PREVIOUSLY DONE ON THE COMPOUNDS INVOLVED.

Camphor.[1] For the purposes of the present investigation common or Japan camphor was used. The first extant record of the existence of this substance, which was unknown to the Greeks and Romans, was made by Aetius of Mesopotamia in the fifth century. This variety which is dextro rotatory is found principally in the so-called camphor tree (Laurus Camphora, Cinnamomum Camphora) which is indigenous to several places in the Orient but principally to Japan and Formosa. It is obtained from the wood of this tree by distillation with steam. It is a white, transparent, slightly waxy solid having a melting point of 178.4°. $(\alpha)_D^{20}$ = 42.22° for a 20 percent alcoholic solution. More than a score of formulas have been proposed for camphor but the one almost universally accepted at the present time was proposed by Bredt[3] in 1893. Bredt's formula follows:



d-Camphoric Acid. d-camphoric acid was first prepared

---

1. For abbreviations used in this paper see J.Am.Ch.Soc.28,1(1906)
2. Beckmann, Ann 250, 352 (1889).
3. Ber. 26, 3047 (1893)

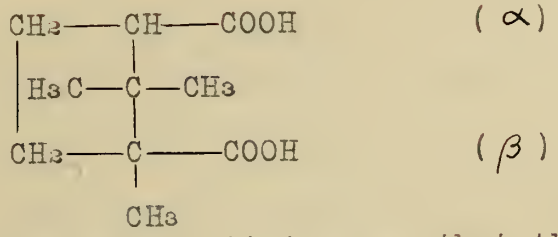
by Kosegarten[1] in 1785 by repeatedly pouring concentrated nitric acid over camphor. It was declared by Dorfurth[2] in 1793 to be identical with benzoic acid, but in 1797 its individuality was demonstrated by Buillon-Lagrange[3]. Although camphoric acid has been made from camphor in a number of other ways, yet its preparation by oxidation with nitric acid has remained the standard method. In 1840 Schwanert[4] heated the camphor with concentrated nitric acid and got a somewhat better yield. Wreden[5] in 1872 improved the method by using a more dilute nitric acid and heating the mixture longer. The latest improvement of much moment was made by Noyes[6] in 1894. After oxidation of the camphor by long heating with dilute nitric acid (1.28) the solution is allowed to cool, the camphoric acid filtered off and the mother liquors, after the addition of concentrated nitric acid to bring the specific gravity up to 1.28, are utilized for the oxidation of more camphor. These mother liquors are utilized in the same manner for the oxidation of a third lot of camphor.

The melting point of camphoric acid in 187. and for a 15 percent solution[7] in acetic acid $(\alpha)_D^{20} = 46{:}66$; for a 15 percent solution[7] in absolute alcohol $(\alpha)_D^{20} = 47.35$. Its

---

1. Roscoe-Schorlemmer, Lehrbuch d. organ. ch. 2, 1170.
2. Aschan, Ch. d. Alicy. Verb. p. 515 (1905).
3. Aschan, Ch. d. Alicy. Verb. p. 515 (1905).
4. Jsb. Chem. 400 (1863).
5. Ann. 164, 323 (1872).
6. Am. 16, 501 (1894)
7. Hartman, Ber. 21, 223 (1888).

formula, which follows directly from that of camphor is



(α)

(β)

From the above formula it is seen that the two carboxyls are differently situated, the one being secondary and the other tertiary. Therefore there is one class of derivatives of camphoric acid which are derivatives of the secondary carboxyl and another which are derivatives of the tertiary carboxyl. The former are known as ortho or alpha (α) derivatives and the latter as allo or beta (β) derivatives. In this paper the symbols α and β will be used. Sometimes it is more convenient to write the cyclic part of the structure simply as C_8H_{14} . When that is done the convention will always be followed of placing the α group above and the β group below. Camphoric acid would therefore be written

(α)

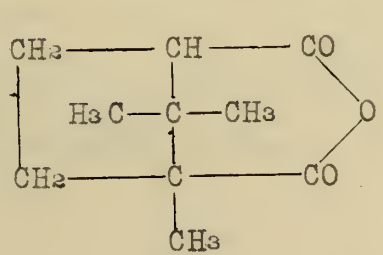
(β)

Camphoric Acid Anhydride. The first report of the preparation of camphoric acid anhydride was made by Buillon-Lagrange[1] in 1799, who prepared it simply by heating the acid. Later it has been prepared from the acid by the action of nearly

---

1. Aschan, Ch. d. Alicy. Verb. p. 502 (1905).

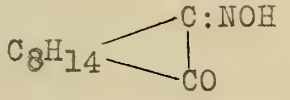
all the reagents which are used for extracting the elements of water from compounds. Probably the most efficient methods are the ones proposed by Noyes[1] and Aschan[2]. Noyes method consists of heating the acid with acetic anhydride and a small amount of acetyl chloride. The method of Aschan is to maintain the acid somewhat above its melting while conducting a current of carbon dioxide through the liquid until no more water passes over. The residue is then distilled. Camphoric anhydride crystallizes from alcohol in long rhombic needles which melt at 220° - 221°. The solution in chloroform shows no optical rotation while a 4.48 percent solution in benzol shows a specific rotation[2] $(\alpha)_j^{18^\circ} = -3.68^\circ$. Its formula follows directly from that of camphoric acid.

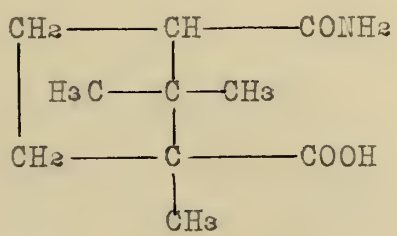


α-Camphoramidic[3] Acid. The first report of the preparation of α-camphor amidic acid was made by Malaguti[4] in 1837. He obtained the acid by heating camphoric anhydride with either liquid or strong ammonia and subsequent precipitation of the free acid from a solution of the ammonium salt with hydrochloric acid. He undoubtedly obtained a mixture of the

---

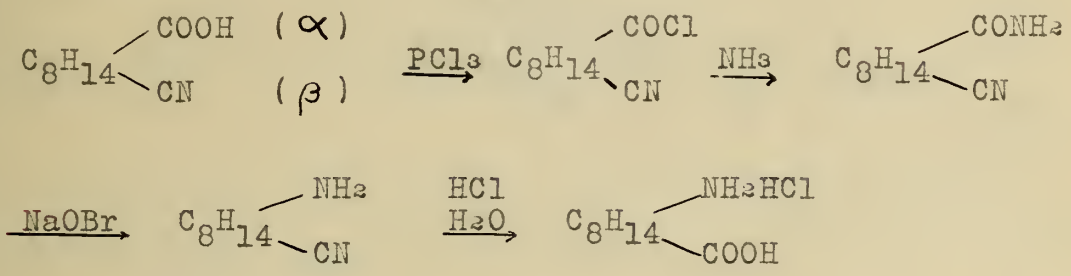
1. Am. 16, 502 (1894)
2. Acta. soc. scient. Fenn. (5),21, 141, 183, (1895)
3. The refers to the position of the amido group.
4. Ann. 22, 43 (1837)

α and β acids. A few years later Laurent[1] obtained the same acid by passing dry ammonia gas into a solution of camphoric anhydride. Of more theoretical importance was its preparation by heating isonitroso camphor[2],  with fuming hydrochloric acid. This demonstrated that the amido group was on the secondary or α carbon. Many other methods of preparation have been used but a discussion of them is not apropos to the present problem. With various modifications the method of Malaguti is still the standard method. Probably the best yields are obtained by the modification of Noyes and Taveau[3], which consists of heating the anhydride with strong ammonia in pressure bottles. 45 to 55 percent. yields were obtained in this manner. The acid crystallizes from water in tablets which melt[4] at 176° - 177°. Its specific rotation[4] $(\alpha)_D$ = 45. for a 6 percent alcoholic solution. Its formula is

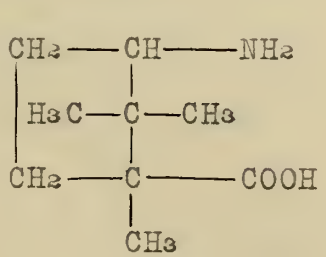


1. Ann. 60, 328 (1846).
2. Claissen u. Manasse Ann. 274, 78 (1893)
3. Am. 32, 287 (1904)
4. Hoogewerf and Van Dorp. Rec. trav. chim. 14, 260 (1895)

Aminocamphonanic acid[1]. This acid was first prepared by Hoogewerf[2]. Noyes[3] quite independently and before anything had been published on the subject, prepared it by treating α-camphoramidic acid with sodium hypobromite. Tiemann[4] has prepared the hydrochloride of aminocamphonanic acid through the following series of reactions:



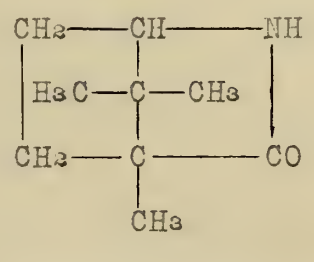
Hoogewerf and Van Dorp found a melting point of 260° for the acid. No report of the specific rotation is to be found in the literature. The results of this investigation on the melting point and specific rotation will be given in Part III of this paper. The formula of the free acid as usually written is,



---

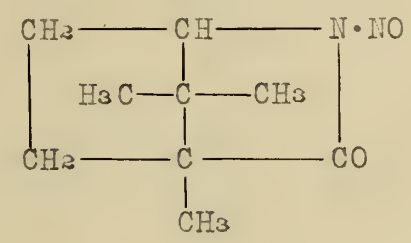
1. For nomenclature see Noyes and Potter, J. Am. Ch. Soc. 34, 1067 (1912).
2. Noyes, Am. 16, 506 (1894) foot note.
3. Noyes, Am. 16, 506 (1894)
4. Ber. 33, 2960 (1900).

Aminocamphonanic Acid Anhydride. This lactam or anhydride was first prepared by Noyes[1] by mixing the hydrochloride of aminocamphonanic acid with quicklime and distilling. Later[2] it was found that it could be just as well prepared by simply heating the free acid to 300°. Of some theoretical interest but no practical use is the preparation of the anhydride reported by Tiemann.[3] He obtained it through the following process. Camphoric α-nitrilic β-acid amide, $C_8H_{14}\begin{matrix}CN\\CONH_2\end{matrix}$ with sodium hypobromite gives a compound whose empirical formula is $C_{10}H_{18}N_2O_3$ and to which Tiemann gives the following formula $C_8H_{14}\begin{matrix}NH\cdot COOH\\CONH_2\end{matrix}$. Upon distillation this acid gives the anhydride of aminocamphonanic acid. The anhydride crystallizes in needles which melt[4] at 203°. Its specific rotation, $(\alpha)_D^{26}$ = -60.1° in a 7 percent alcoholic solution. Its formula is,

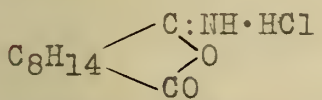


1. Am. 16, 507 (1894)
2. Noyes and Taveau Am. 32, 287 (1904)
3. Ber. 33, 2960 (1900)
4. Noyes, Am. 16, 507 (1894)

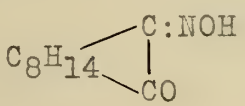
Nitroso Derivative of the Anhydride of Aminocamphonanic Acid. This compound was first prepared by Bredt[1] in 1902, by treating the hydrochloric solution of the aminocamphonanic acid with nitrous acid. Its melting point[1] is 138° - 139°. Its formula is



Cyanocamphonanic Acid. Hoogewerf and Van Dorp[2] were the first to report the preparation of this material. They prepared it by treating the α-camphoramidic acid with acetyl chloride. The α-camphoric isoimide hydrochloride,



which was formed was slowly added to 12 percent ammonia. From the solution the cyanocamphonanic acid was precipitated with hydrochloric acid, and was purified by recrystallization from hot water. Oddo and Leonardi[3] prepared it by treating isonitroso camphor

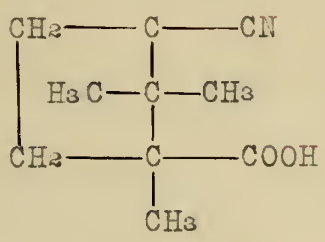


, with phosphorous trichloride, phosphorous pentachloride, acetic anhydride, or acetyl chloride. The melting point[4] of the acid is 151° - 152°,

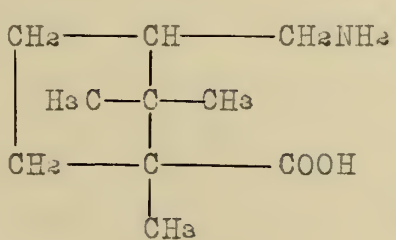
---

1. Ber. 35, 1291 (1902)
2. Rec. trav. chim. 14, 262 (1895)
3. Gazz. chim. ital. (1), 26, 409 (1896)
4. Rec. trav. chim. 14, 262 (1895)

and for a 6% solution in alcohol the specific rotation[1] $(\alpha)_D = 67.3°$. Its formula is

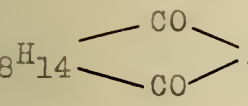


α-aminocampholic acid. No report of the preparation of the free acid is to be found in the literature. Hoogewerf and Van Dorp[2] prepared the chloroplatinate and the Italian chemists[3] mentioned above prepared the hydrochloride and give its melting point as 268° - 270°. Rupe and Splittgerber[4] also prepared the hydrochloride and give its melting point as 247° - 248°. In all cases the salts have been prepared by reducing cyanocamphonanic acid with sodium and alcohol. The formula which would be ascribed to the free acid is

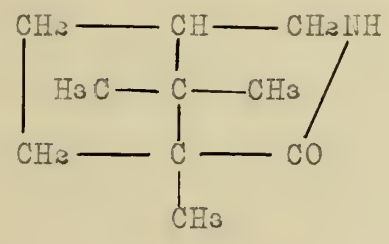


1. Rec. trav. chim. 14, 264 (1895)
2. Rec. trav. chim. 14, 264 (1895)
3. Gazz. chim. ital. (1), 26, 409 (1896)
4. Ber. 40, 4311 (1907)

α-camphidon. This substance along with β-camphidon was first prepared and analyzed by Tafel and Eckstein[1] in 1901 by the electro reduction of camphoric acid imide,



C_8H_{14} CO, CO, NH. It was probably prepared by Oddo and Leondari[2] in 1896 by heating the hydrochloride of the α-aminocampholic acid but they give no analyses or none of the constants of the substance. Rupe and Splittgerber[3] prepared it by heating the hydrochloride and they give its analyses and other constants. Its melting point[4] is 230° - 232° and its specific rotation $(\alpha)_D$ = -37.2 in 10% benzol solution.

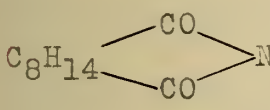


β-camphoramidic acid. Although it is undoubtedly true that in all the methods for the preparation of the α-camphoramidic acid which involved the treatment of camphoric acid anhydride with ammonia that at least a small amount of β-camphoramidic acid was formed, yet it was not until 1895 that a small quantity[5] was separated from the crude α-camphoramidic acid obtained from camphoric acid anhydride

---

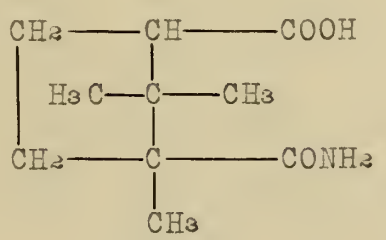
1. Ber. 34, 3278 (1901).
2. Gass. chim ital. (1), 26, 409 (1896).
3. Ber. 40, 4311 (1907).
4. Tafel and Eckstein. Ber. 34, 3278 (1901).
5. Hoogewerf and Van Dorp. Rec. trav. chim. 14, 267 (1895).

and ammonia. It was, however, discovered the year before[1] by the same men and quite independently by Noyes,[2] as the product of the treatment of camphoric acid imide,



C_8H_{14} (CO)$_2$NH, with sodium hydroxide solution.

Its practical preparation from camphoric acid anhydride and ammonia was worked out by Noyes and Taveau[3]. In their method for the preparation of the α-camphoramidic acid, after treating the camphoric acid anhydride with strong ammonia and filtering off the ammonium salt of the α-acid from the cooled solution, if strong sodium hydroxide solution is added to the filtrate the sodium salt of the β-acid is precipitated. The acid crystallizes in leaves which melt[4] at 182° - 183°. The specific rotation[5] $(\alpha)_D$ = 60° for a 6 percent alcoholic solution. Its formula is

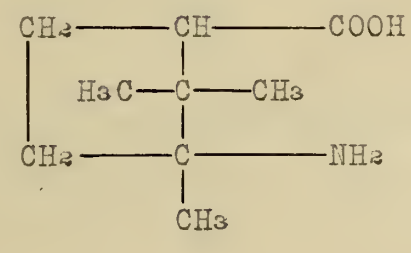


Dihydroaminocampholytic Acid. Noyes[6] was the first to prepare this acid. The method which he worked out is

---

1. Pr. Dutch. Acad. of Scien. Jan. 27, 1894.
2. Am. 16, 309 (1894).
3. Am. 32, 287 (1904).
4. Noyes. Am. 16, 310 (1894).
5. Hoogewerf and Van Dorp. Rec. trav. chim. 14, 266 (1895)
6. Am. 16, 310 (1894).

essentially the same as is used at present. This involves the treatment of the sodium hydroxide solution of the α-camphoramidic acid with sodium hypobromite. The acid crystallizes from water in white plates which sublime without melting upon heating. The original method of preparation has been somewhat improved.[1] $(\alpha)_D = 53.7°$ for the saturated solution.[2] Its formula is,

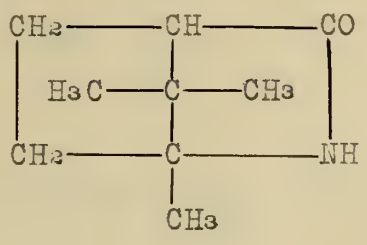


Dihydroaminocampholytic Acid Anhydride. This substance was first prepared by Noyes[3] by heating the hydrochloride of of dihydroaminocampholytic acid with quick lime. Bredt[4] prepared the same substance by heating the free amino acid with acetic anhydride. Tiemann[5] prepared it in a manner similar to his preparation of the anhydride of aminocamphonanic acid. He started with camphoric β-nitrilic α-amidic acid $C_8H_{14}(CONH_2)(CN)$ which with sodium hypobromite gives a compound to which he ascribes the formula $C_8H_{14}(CONH_2)(NH\cdot COOH)$.

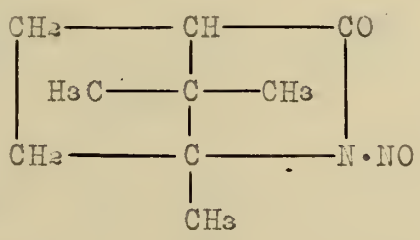
---

1. Noyes, 16, 503, (1894).
2. Noyes and Phillips. Am. 24, 290 (1900).
3. Am. 16, 504 (1894).
4. Ann. 314, 392 (1900).
5. Ber. 33, 2960 (1900).

This upon distillation gives the anhydride of dihydroaminocampholytic acid. Its melting point[1] is 188° - 189° and its specific rotation[2] $(\alpha)_D^{30}$ = 72.8, 1.0 gram in 10 c.c. of petroleum ether solution. Its formula is



Nitroso Derivative of Dihydroaminocampholytic Acid Anhydride. The nitroso derivatives was first prepared by Bredt[3] by treating the dilute hydrochloric acid solution with nitrous acid. He gives no report of its properties. Its melting point[4] is 188° - 189°. Its formula is,

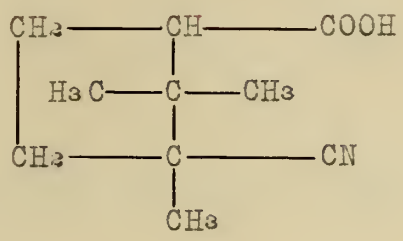


Dihydrocyanocampholytic Acid. This acid was first prepared by Hoogewerf and Van Dorp[5] from β-camphoramidic acid in just the same way as they prepared cyanocamphonanic acid from α-camphoramidic acid. They give the melting point as

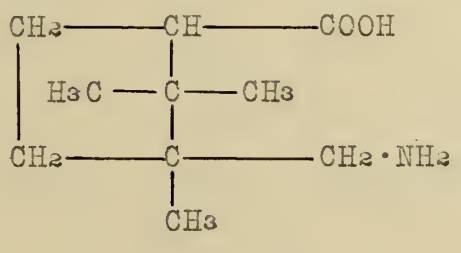
---

1. Noyes. Am. 16, 504 (1894)
2. Noyes and Potter. J. Am. Ch. Soc. 34, 1072 (1912)
3. Ann. 314, 392 (1900)
4. Noyes and Potter. J. Am. Ch. Soc. 34, 1072 (1912)
5. Rec. trav. chim. 14, 267 (1895)

109° - 110° and its specific rotation $(\alpha)_D$ = 18.12° for a 6 percent solution in benzol. Its formula is,



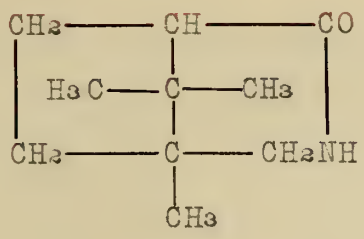
β-aminocampholic Acid. The free acid has never been prepared, but the hydrochloride was prepared by Rupe and Splittgerber[1] by the reduction of dihydrocyanocampholytic acid with alcohol and sodium. They give the melting point of the hydrochloride as 215° - 220°. Its formula is,



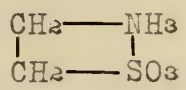
β-camphidon. This compound was first prepared along with the α-camphidon by Tafel and Eckstein[2] by the electro reduction of camphoric acid imide. It was later prepared by Rupe and Splittgerber[3] by heating the hydrochloride of β-aminocampholic acid. They report a melting point of 225° and its specific rotation $(\alpha)_D$ = 66.5 for a 10 percent benzol solution. Its formula is,

---

1. Ber. 40, 4317 (1907)
2. Ber. 34, 3274 (1901)
3. Ber. 40, 4317 (1907)



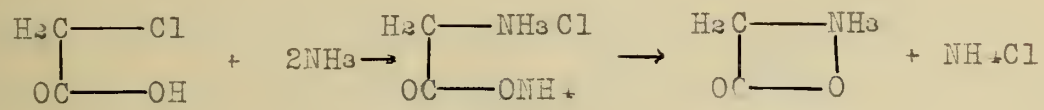
2. THE STRUCTURE OF THE AMINO ACIDS.

In 1875 Erlenmeyer and Sigel[1] suggested that since in amino acids there is both a basic and an acidic group, there might be an inner salt structure. Thus amino caprylic acid would have the structure . They had proposed[2] the same thing concerning taurin  in 1867. In 1885 Ostwald[3] noticed that a solution of glycocoll CH_2CHNH_2COOH had a very low molecular conductivity and that this was only very slightly increased with dilution. He said that it was more like a neutral salt in its behavior than like an acid. In 1891 Marckwald[4] and others called attention to the fact that amino acids of the aliphatic series react only very slowly with mustard oils to form thioureas, while all other primary amines react very readily. Because of this fact and also because of the fact that the amino acids in alkaline solution react very readily with the mustard oils

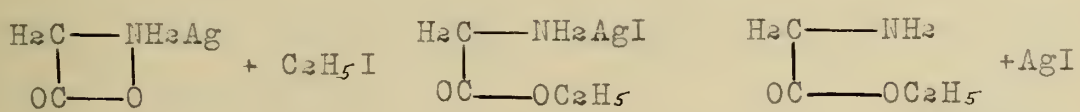
---

1. Ann. 176, 349 (1875)
2. Verb. d. natur. med. Ver. Heid. 1867.
3. J. pr. Ch. 32, 369 (1885)
4. Ber. 24, 3278 (1891)

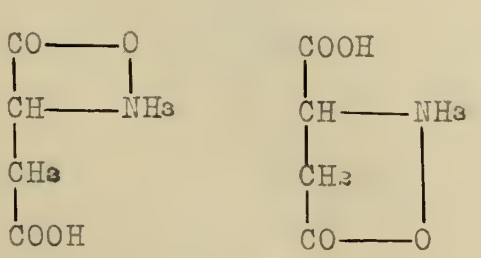
these investigators hold that the amino acids are in reality inner salts. Sakurai[1] attempts to substantiate the inner salt structure from a consideration of the method of formation of the amino acids. He takes as an example the formation of glycocoll from acetic acid and ammonia. The mechanism, according to him, is as follows:



Even substances like hippuric acid, he says, must have the inner salt structure. This view is substantiated by the fact that hippuric acid and other amino acids resist attempts to change them into acid chlorides. He explains the esterification of glycocoll as follows, giving silver glycocoll the formula as indicated,



He also says that a second aspartic acid will be isolated. The formulas of the two will be,



1. Pr. Ch. Soc. No. 138 (1894)

Walker[1] in a reply to Sakurai states that physical methods will throw very little light on the problem except that molecular weight determinations will show whether a single or double molecule is present in a solution of the substance. Glycocoll, for instance, has the normal molecular weight. Conductivity experiments tell us very little about glycocoll and other unsubstituted amino acids but for substances like phenyl glycocoll, $NHC_6H_5CH_2COOH$, conclusive evidence is given from conductivity data that it is not an inner salt. Walker attempts to substantiate this statement as follows: Acetic acid has a dissociation constant, K_a = 0018. This is many times greater than the constant for glycocoll. Phenyl glycocoll has a constant, K_a = .0042, so that the introduction of a phenyl group in place of one of the hydrogens in the amino group has raised the conductivity above that of acetic acid. Consequently, if acetic acid contains a carboxyl group, phenyl glycocoll must, a fortiori, contain one.

In 1895 Tilden and Forster[2] found that amino acids reacted readily with nitrosyl chloride, exchanging the amino group for a chlorine atom. They take this as being opposed to the theory of an inner salt structure. In 1897 Carrara and Rossi[3] said that the theory of the inner salt structure was supported by the following considerations. Upon dissolving

---

1. Pr. Ch. Soc. 10, No. 139 (1895)
2. Chem. News, 71, 239, (1895)
3. Atti Reale Accad. Lincei. (5) 6 (1897)

betain hydrochloride in water, the chlorine is ionized off and this causes an equivalent quantity of hydrogen ions to be formed from the hydrochloride. The betain residue will then combine to form the anhydrous form, and from analogy the unsubstituted amino acids would do the same. This view was worthless from the fact that it had already been shown[1] that the molecular conductivity of betain hydrochloride is only about one-half that of hydrochloric acid.

This account of the views held concerning the structure of amino acids brings us up to the time when the electrolytic and hydrolytic theories were beginning to be better understood. Bredig[2] in 1889 indicated the various equilibrium equations that one must consider in a study of the amino acids. In 1901 Winkelblech[3] applied the hydrolytic equation for the salt of a weak acid and a weak base to the amino acid, assuming that the degree of ionization is the same as for an ordinary salt such as ammonium acetate. Walker[4] in 1904 systemitized the formulation of the equilibrium equations in regard to amphoteric electrolytes. The formulation of Winkelblech and Walker and of some later workers will be given and discussed in Part II of this paper.

"Zwitterion". Both Bredig[2] and Winkelblech[3] mention

---

1. Bredig Z. physik. Ch. 13, 194 (1894)
2. Z. Elektrochem. 6, 33 (1899)
3. Z. physik. ch. 36, 592 (1901)
4. Pr. Roy. Soc. 74, 155 (1904); 75, 271 (1905)

the possibility of there being "zwitterion" in the solution of an amino acid. The existence of the "zwitterion", an ion with both a negative and a positive charge, was first proposed by Küster as being present in a solution of methyl orange. He considers both the basic and acidic groups as being strong and that the two ends of the organic ion are too far apart to unite. The "zwitterion" would be $^{+}NH(CH_3)_2C_6H_4N_2C_6H_4SO_3^{-}$ This complex is colored weakly red and it ionizes very slightly, thus:

$$H^{+} + N(CH_3)_2C_6H_4N_2C_6H_4SO_3^{-}$$

This anion is intensely yellow so that an excess of alkali will cause the production of an abundance of the anion. Although this view of the mechanism of the action of methyl orange as an indicator is not held at the present time yet no one has shown that a "zwitterion" is incapable of existence.

PART II.

THEORETICAL.

P A R T II.

T H E O R E T I C A L.

1. CONDITIONS FOR INNER SALT FORMATION IN AMINO ACIDS.

Amphoteric electrolytes. Following is a summary of the fundamental equations for amphoteric electrolytes as given by Winkelblech[1] and Walker.[2] In a solution of an amphoteric electrolyte there will be the following forms. Let the small letters represent the active masses.

H^+	OH^-	XOH^-	HX^+	HXOH	X
a	b	c	d	e	f

e is always proportional to f no matter what the total concentration. This is apparent from a consideration of the mass law for e and f. It can also be proved from the following relations, where K_w = dissociation constant for water, K'_a = true dissociation constant for the acid, K'_b = true dissociation constant for the base, and Q = a constant.

$$a\,b = K_w \quad (1); \qquad a\,c = K'_a\,e \quad (2); \qquad b\,d = K'_b\,e \quad (3);$$

$$c\,d = Q\,f^2 \quad (4).$$

Multiply (2) by (3) $\qquad a\,b\,c\,d = K'_a K'_b e^2 \quad (5)$

---

1. Z. physik. Chem. 36, 590 (1901)
2. Pr. Roy. Soc. 73, 155 (1904); 74, 271 (1905).

Substituting from (1) and (4),

$$K_w\ Qf^2 = K'_a K'_b e^2 \qquad (6)$$

Therefore e and f are always in a constant ratio no matter what the concentration.

Although Winkelblech[1] mentions the possibility of there being a "zwitterion" in the solution yet such a complex has never been formulated in the equilibrium equations for amphoteric electrolytes. This will now be done. In the solution there will be the following forms, again letting the small letters represent the active masses.

H^+	OH^-	XOH^-	HX^+	HXOH	X	$^-X^+$
a	b	c	d	e	f	g

For this case equations (1), (2), (3), and (4) will hold and in addition we will have, where S is a constant

$$c\ d = S\ g^2 \qquad (7)$$

Substituting (1) and (7) in (5) we get

$$K_w\ S\ g^2 = K'_a K'_b e^2 \qquad (8)$$

Therefore g and e are always in a constant ratio and since the same was proven to be true for e and f, then e is proportional to the sum of f and g; therefore, where,

$$u = e+f+g \qquad (8a)$$

---

1. Z. physik. 36, 590 (1901)

from equations (2), (3) and (8a)

$$a\ c = K_a\ u \quad (9); \qquad b\ d = K_b\ u \qquad (10)$$

The constants K_a and K_b are different than K'_a and K'_b. The former are accessible of measurement while the latter usually are not, as is pointed out by Lunden.[1]

From equations (1) and (10)

$$d = \frac{K_b}{K_w}\ u\ a \qquad (11)$$

and from (1) and (9)

$$c = \frac{K_a}{K_w}\ u\ a \qquad (12)$$

The following must be true

$$a + d = b + c \qquad (13)$$

Substituting the values of c and d from (12) and (11) in (13) we get,

$$a\left(1 + \frac{K_b}{K_w}\ u\right) = b\left(1 + \frac{K_a}{K_w}\ u\right) \qquad (14)$$

Now suppose the solution of the substance is neutral to litmus. Then we will have a = b and therefore c = d, and from (14) $K_a = K_b$. Then if a solution of the substance had a very low specific conductance say of the order of

---

1. J. Bi. Ch. 4, 267 (1908)

magnitude of 10^{-5} mhos there would be very few current bearing ions in the solution, or in other words c and d will be very low. Suppose, where

$$u + d + c = 1$$

$$c = d = .01$$

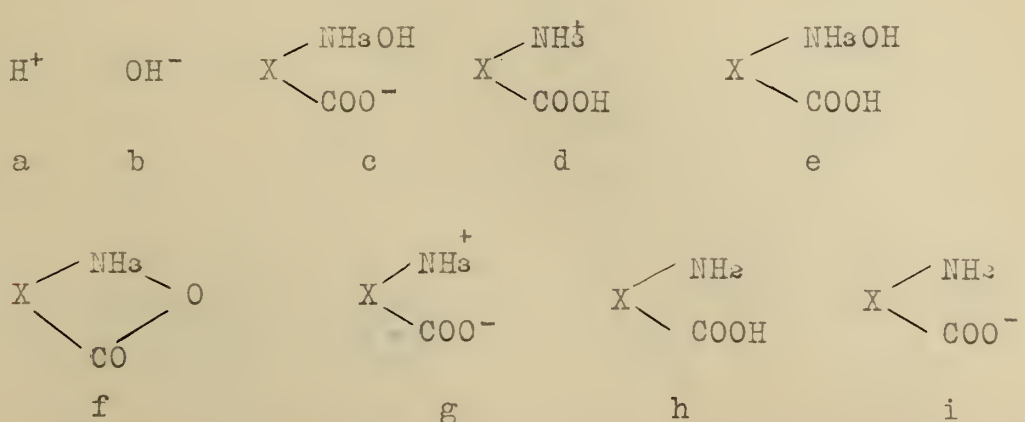
$$\text{then} \qquad u = 1 - (c+d) = 1 - .02 = .98$$

For purposes of approximation we may take $K_W = 10^{-14}$, so from (11)

$$.01 = \frac{K_b}{10^{-14}} \quad (.98)\ (10^{-7})$$

$$K_b = 10^{-9} = K_a \qquad (15)$$

Amino Acids. Having shown some of the relations exhibited by ordinary amphoteric electrolytes, the theory will now be applied to amino acids, which, since they contain both a basic and an acidic group are amphoteric in character. In a solution of an unassociated amino acid there are the following possibilities,



Just as in a water solution of ammonia there is a considerable quantity present as NH_3 so in an aqueous solution of an amino acid the possibility of forms h and i must be considered.

Since the acid and basic constants which are accessible of measurement, as has been pointed out by Lunden[1], are not the true constants but for base would be

$$b\,d = K_b\,(e + f + g + h)$$

there is no way of telling in just what form the unionized portion exists . But it is apparent that if the basic and acidic groups are quite weak that form g can only be present in very small concentration for it would as fast as formed combine with the hydrogen and hydroxyl of water. Therefore the strength of our acidic and basic groups would largely depend upon the tendency of form f to ionize or perhaps a better term, to polarize.

In the same manner as has been shown for an ordinary amphoteric elextrolyte, where

$$e + h = u \qquad (16)$$

then $$a(c + i) = K'_a\,u \qquad (17)$$

$$b\,d = K'_b\,u \qquad (18)$$

$$a\,b = K_w \qquad (1)$$

---

1. J. Bi. Ch. 4, 267 (1908)

Since we have here an inner salt we will develop the hydrolysis equation for this form, f. Divide equation (1) by the product of (17) and (18) and we get

$$\frac{u^2}{d(c+i)} = \frac{K_w}{K_a K_b} \qquad (19)$$

Now where h = degree of hydrolysis and C_s = concentration of the whole substance

$$u = h\,C_s \qquad (20)$$

And if the strength of both acid and base are of the order of magnitude $K_a = K_b = 10^{-9}$

$$d = (c+i) = Y_s\,(1-h)\,C_s \qquad (21)$$

Where Y_s = the degree of ionization of a salt character.

Substitute (20) and (21) in (19) and we get

$$\frac{h^2}{(1-h)^2 Y^2} = \frac{K_w}{K'_a\,K'_b} \qquad (22)$$

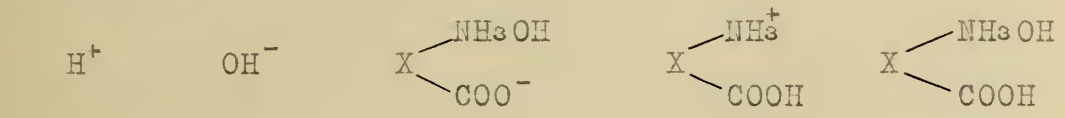
Winkelblech[1] applied equation (22) to amino acids, assuming a value of .9 for Y. But K'_a and K'_b are not the constants which are accessible of measurement and the above equation can only be true when f and g are negligible when compared to e and h. This is only true when the degree of

---

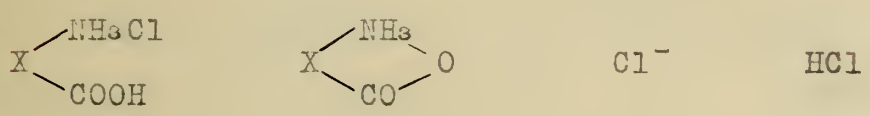
1. Z. physik. Chem. 36, 592 (1901). The formula he used

polarization of f, that is, its tendency to pass into g is practically one. This will be more fully discussed later.

Hydrochlorides of Amino Acids. In a solution of the hydrochloride of an amino acid[1] we will have the following possibilities,



a b c d e



f g h i

The amount of form g present will depend upon the degree of polarization. The less this degree of polarization the more of g will be present and the greater will be the degree of hydrolysis as measured by finding the concentration of the hydrogen ion. In dilute solutions form f will be largely ionized to d and h. Practically none of c will be

---

was $\frac{h^2}{(1-h)^2(55.5\ Y^2)} = \frac{K_w}{K_a K_b}$. The equation above is just the same as was used by him for his K_w value was $\frac{1}{55.5}$ that ordinarily used.

---

1. Lunden (J. Bi. Ch. 4, 267 (1908) has worked this out very completely. Only the essential points will be given.

present due to the high concentration of hydrogen ion. The amount of form e present will depend upon the inherent strength of the acidic and basic groups and upon the degree of polarization of g.

Sodium Salts of Amino Acids. If the solution of the amino acid is neutral to litmus, as shown above, the basic and acidic groups must be equal in strength. Therefore what has been said in regard to the hydrochlorides may be said, with obvious modifications, of the sodium salts.

Aminocamphonanic, dihydroaminocampholytic, and α- and β- aminocampholic acids. In the preceeding we have discussed the dissociation and hydrolysis of amino acids and their salts, whose acidic and basic constants were approximately equal to each other and equal to 10^{-9}. We will now bring the discussion to bear directly upon amino-camphonanic acid and dihydroaminocampholytic acid. A solution of either of these acids is quite neutral to litmus. Conductivity experiments were made on .175 N solutions of both acids and each solution showed a specific conductivity only about three times greater than that of the water used, the specific conductivity of the latter being 3×10^{-6} mhos. The acids were purified by recrystallizing the already fairly pure acids six times from water.[1] Therefore it may be said with surety that only a very small percent of the acids are

---

1. Walker (Pr. Roy. Soc. 74, 278 (1905) states that it was found necessary to recrystallize asparagin, considered pure in an ordinary analytical sense, twenty five times before a minimum conductivity was given.

present in the solution as current bearing ions. It was shown in the discussion preceding, from these facts regarding the two acids that the dissociation constant for the acidic and basic groups must be 10^{-9} or less. Although we have no very direct evidence as to the lower limit for this value, yet the following may be taken as indicating that the value for both the acidic and basic constants is not much less than 10^{-9}.

In dihydroaminocampholytic acid and aminocamphonanic acid we have a secondary and tertiary carboxyl respectively. No cyclic acids resembling these two acids, whose dissociation constant had been obtained[1], could be found. The acids most nearly resembling these, whose constants have been determined, are trimethyl acetic acid whose constant is 9.78×10^{-6}, and methyl ethyl acetic acid whose constant is 1.7×10^{-5}. Now the introduction of an amino group into propionic acid in the α position lowers the acidic constant from 1.40×10^{-5} to 1.9×10^{-10} and introducing an amino group into acetic acid lowers the constant from 1.8×10^{-5} to $1.8 \cdot 10^{-10}$. But in aminocamphonanic and dihydroaminocampholytic acids the amino group is in the γ position as has been pointed out by Derick[2], the effect in the γ position of a positive group on a negative group is not so marked as is the effect in the α position. Therefore we may say with some degree of surety that our acids have a dissociation constant not much less than 10^{-10}.

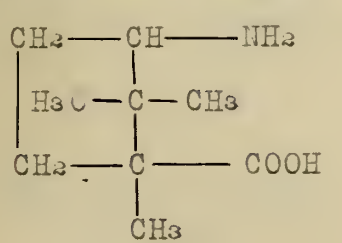
---

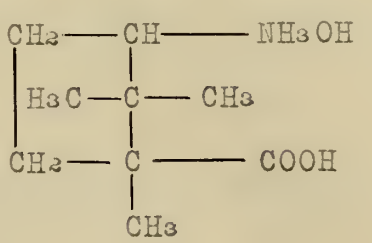
1. All the dissociation constants are taken from Lunden (Samm. Ch. Ch.-tech. Vortrage 14, 1 (1909).
2. J. Am. Ch. Soc. 33, 1167 (1911)

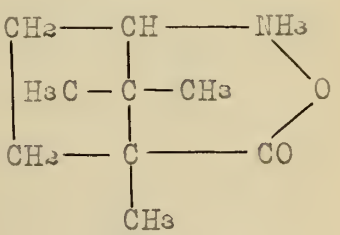
We will now consider the basic groups. Dissociation constants are not known for any amino acids resembling the amino acids under investigation but the following line of reasoning throws some light on the subject. The basic constant for methyl amine is $5 \cdot 10^{-4}$. The basic constant of glycocoll, in which the carboxyl group replaces a hydrogen atom in methyl amine, is $1.8 \cdot 10^{-12}$. Although no data is available it is undoubtedly true that the effect of the negative carboxyl group upon the positive amino group would be very much less in the γ than in the α position. These facts, of themselves, are not very convincing, but coupled with the fact that the acid and basic constants must be approximately equal there seems to be little doubt but that the two dissociation constants be very closely around 10^{-9} to 10^{-10}.

In view of what has been said concerning amino-camphonanic acid and dihydroaminocampholytic acid and their salts, those forms which directly effect polarized light which are present in appreciable quantities will now be put down.

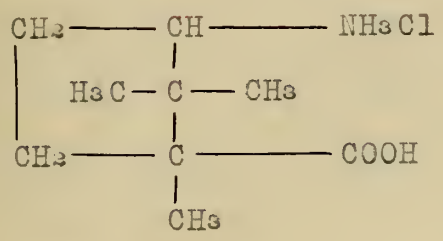
Aminocamphonanic acid.

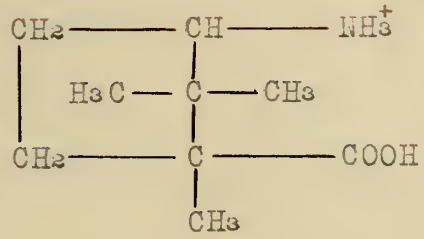




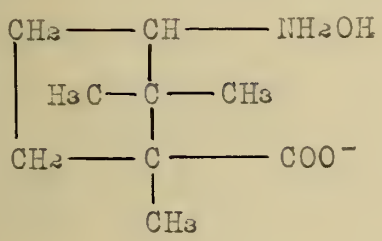


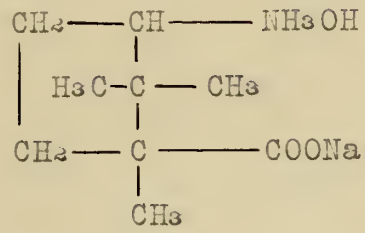
Aminocamphonanic acid hydrochloride.

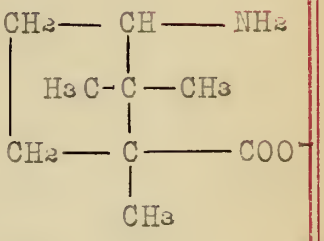


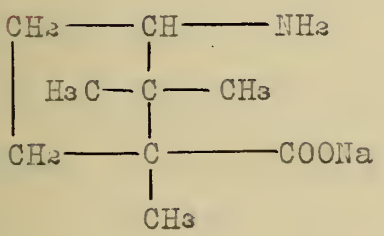


Sodium salt of aminocamphonanic acid.

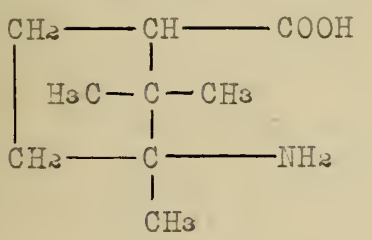


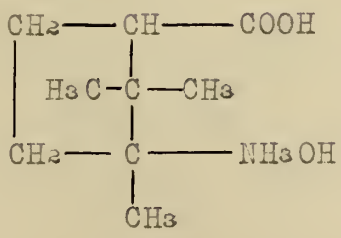


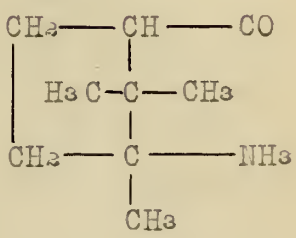




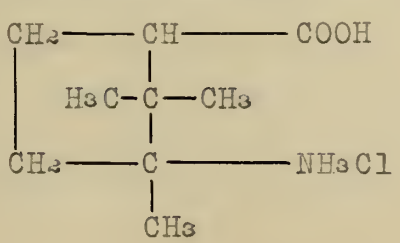
Dihydroaminocampholytic acid.

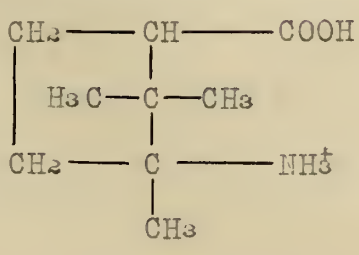




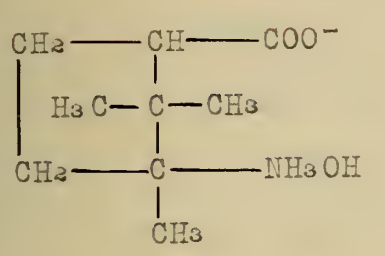


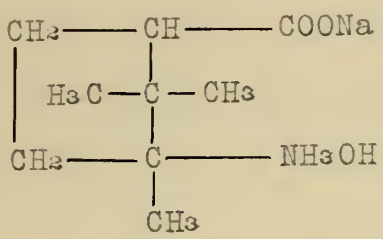
Dihydroaminocampholytic acid hydrochloride.

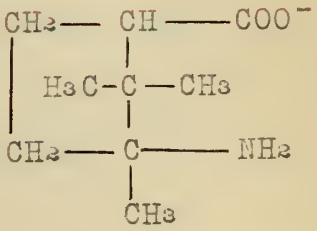


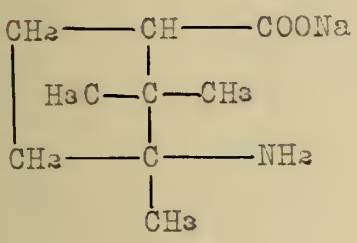


Sodium salt of dihydroaminocampholytic acid.







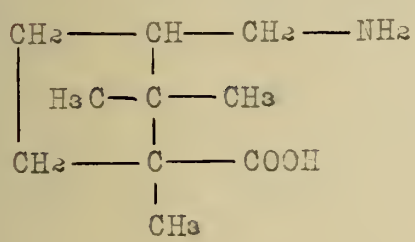


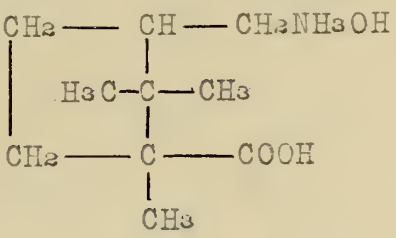
The only condition under which we could have an appreciable quantity of the inner salt present in a solution of the hydrochloride or the sodium salt would be for the degree of polarization of the inner salt to be approximately equal to or less than the basic and acid constants. That this is not true is shown by the fact that the hydrochloride are easily isolated and from a comparison of the rotations. To most surely show this a conductivity method could be devised.

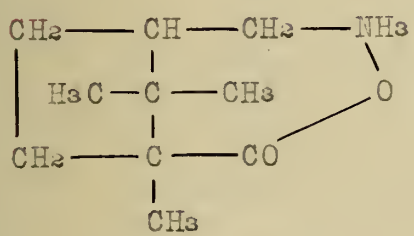
Since α and β aminocampholic acids are slightly alkaline to litmus and not enough of either acid was obtained sufficiently pure to find the conductivity of their solutions nothing very definite can be said in regard to them. But it is probable that the strength of their acid and basic groups are not far from the strength of the acid and basic groups of aminocamphonanic anddihydrocampholytic acids, the basic

group being perhaps somewhat stronger and the acidic group somewhat weaker. If this is true their solutions, together with the solutions of their salts contain principally the forms similar to the ones above. Just the forms for the free acids will be tabulated here.

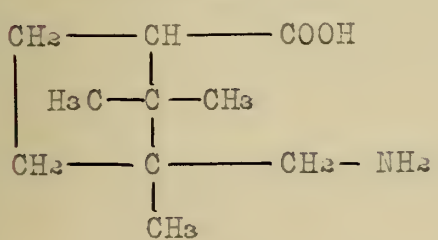
α- aminocampholic acid.

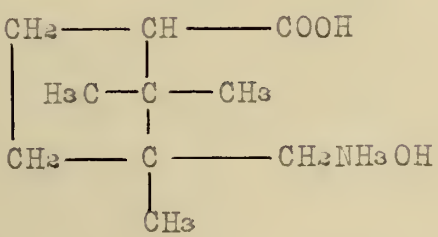






β - aminocampholic acid.





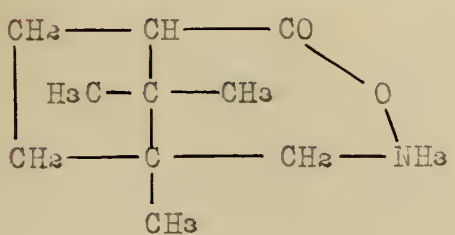


TABLE I.

I	II	III	IV	V	VI
No.	Composition of Solution	N	$(\alpha)_D$ (cal.)	$(\alpha)_D$ (act.)	Temp.
1	.5 gr. α-aminocampholic acid hydrochloride	.226	53.3	44.7	24
2	.207 gr. α-aminocampholic acid	.112	67.	67.	26
3	.5 gr. α-aminocampholic acid hydrochloride + 1 mol. NaOH	.226	62.4	62.4	24
4	.5 gr. α-aminocampholic acid hydrochloride + 2 mol. NaOH	.226	65.6	58.6	25
5	.104 gr. α-aminocampholic acid + 1 mol. NaOH	.056	67.0	59.9	23
6	.5 gr. β-aminocampholic acid hydrochloride	.226	49.5	41.3	26
7	.25 gr. β-aminocampholic acid	.200	16.4	16.4	25
8	.5 gr. β-aminocampholic acid hydrochloride + 1 mol. NaOH	.226	16.7	16.7	27
9	.25 gr. β-aminocampholic acid hydrochloride + 2 mol. NaOH	.113	15.2	13.6	26
10	.25 gr. β-aminocampholic acid + 1 mol. NaOH	.135	16.0	14.3	27
11	.5 gr. aminocamphonanic acid	.292	-29.2	-29.2	25
12	1.0 gr. aminocamphonanic acid hydrochloride	.48	30.3	25.0	24
13	1.0 gr. aminocamphonanic acid + 1 mol. NaOH	.584	59.3	52.8	24
14	.5 gr. aminocamphonanic acid + 2 mol. NaOH	.292	58.6	52.2	24
15	1.0 gr. aminocamphonanic acid hydrochloride + 1 mol. NaOH	.48	-28.8	-28.8	25
16	1.0 gr. aminocamphonanic acid hydrochloride + 2 mol. NaOH	.48	55.4	49.1	27

I	II	III	IV	V	VI
No.	Composition of Solution	N	$(\alpha)_D$ (cal)	$(\alpha)_D$ (act)	Temp.
17	1.0 gr. aminocamphonanic acid hydrochloride + 2.25 mol. NaOH	.48	54.3	48.2	26
18	1.0 gr. aminocamphonanic acid hydrochloride + .5 mol. HCl	.48	30.5	25.2	27
19	.75 gr. dihydroaminocampholytic acid.	.438	53.7	53.7	24
20	.5 gr. dihydroaminocampholytic acid	.292	54.7	54.7	25
21	1.0 gr. dihydroaminocampholytic acid hydrochloride	.48	50.1	41.3	26
22	1.0 gr. dihydroaminocampholytic acid + 1 mol. NaOH	.48	20.7	18.3	23
23	.5 gr. dihydroaminocampholytic acid hydrochloride + 1 mol. NaOH	.24	54.0	54.0	24
24	1.0 gr. dihydroaminocampholytic acid hydrochloride + 2 mol. NaOH	.584	20.5	18.2	25
25	1.0 gr. dihydroaminocampholytic acid hydrochloride + .5 mol. HCl	.48	48.7	40.1	26

In Table No. II some of the values from Table No. 1 are put in a somewhat different form. All the values for $(\alpha)_D$ are calculated from the basis of free amino acid present in the solution.

TABLE II.

NO.		Free Acid $(\alpha)_D$	HCl Salt $(\alpha)_D$	Na Salt $(\alpha)_D$
26	α-aminocampholic acid	67.	53.3	67.
27	Aminocamphonanic acid	-29.2	30.3	59.3
28	Dihydroaminocampholytic acid	53.7	50.1	20.7
29	β-aminocampholic acid	16.4	49.5	16.7
30	Iso dihydroaminocampholytic acid[1]	-32.9	-54.7	

Discussion of Tables I and II. In Tables I and II the rotations[2] of the four amino acids, together with the rotations of their hydrochlorides and sodium salts, are given. In Table I, column I gives the number of the experiment, II gives the amount of material in 10 c.c. of solution, III gives the normality with respect to the respective free acid present, IV gives the specific rotation with respect to the respective free acid present, V gives specific rotation of the form actually present, without regard to hydrolysis or the like. VI gives the temperature of the solution when the rotation was taken. It is to be understood that when the term free amino acid is used that the form that the solid acids have is meant, that is, $X(NH_2)COOH$, without regard to actual structure. The rotations given in Table II are all calculated the same as the rotations in column IV.

Perhaps the most striking thing concerning the value

---

1. L. F. Nickell. Ph.D. Thesis 1913.
2. More details concerning the method of taking the rotations are to be found in Part III.

of the rotations as shown in the above tables is that numbers 11 and 15, which show the rotations of the free aminocamphonanic acid to be negative while every other value is positive. Perhaps the difference between aminocamphonanic acid and the other acidsis more plainly shown in Table II. The very great difference between the value for the free aminocamphonanic acid and its hydrochloride and sodium salt is totally dissimilar to the relations of the other acids to their salts. How are we to account for this great difference? For weak acids with a fairly low molecular weight the rotations of the free acid and the sodium salts seem to be quite different[1] but for acids with a higher molecular weight they seem to be more nearly equal.[2] This relation has also been worked out by Hartman[3] for camphoric acid and its salts. He found the following results, all at 20°.

Camphoric acid

$(\alpha)_D = 46.4$ 10.5 per cent solution in acetic acid.

$(\alpha)_D = 50.8$ 13.7 per cent solution in acetone.

$(\alpha)_D = 47.4$ 16.9 per cent solution in alcohol.

For the neutral sodium salt of camphoric acid

$(\alpha)_D = 16.9$ 10.0 per cent solution in water

Calculated for the acid present

$(\alpha)_D = 20.6$

---

1. Schneider Ann. 207, 257 (1881)
2. Rimbach Z. physik. Ch. 28, 249 (1899)
3. Ber. 21, 221 (1888)

From these relations, namely, that the specific rotation of camphoric acid and its sodium salt is positive and not so far different from the acid and that the hydrochlorides and sodium salts of the four acids are positive and the specific rotations of the free acids with the exception of aminocamphonanic acid lead to the view that, in a solution of the free aminocamphonanic acid we had in the main, an inner salt structure and that the other acids do not.

This inner salt structure can only be due to a slight degree of polarization, as has been indicated. This undoubtedly causes the basic and acidic groups to be considerably weaker yet the degree of polarization is not so small but that only a small portion of the inner salt is present in a solution of the hydrochloride or sodium salt, as is apparent from the rotations.

The results obtained on the molecular weights of the four amino acids, together with the results obtained for isodihydroaminocampholytic acid by L. F. Nickell,[1] will now be given and their bearing upon the problem discussed.

α -aminocampholic acid

Gr. Acid	Gr. Water	ΔtF	MW	Cal. for $C_8H_{14}\begin{matrix}CH_2\cdot NH_2\\COOH\end{matrix}$
.418	15.6	.251	196	185
.585	18.4	.297	197	

Aminocamphonanic acid — Cal. for $C_8H_{14}\begin{matrix}NH_2\\COOH\end{matrix}$

.304	16.6	.194	173	171
.743	19.2	.409	174	

1. Ph.D. Thesis 1913

Dihydroaminocampholytic acid

Cal. for C_8H_{14}(NH$_2$)(COOH): 171

Gr. Acid	Gr. Water	ΔtF	MW
.415	20.5	.199	187
.613	21.2	.278	191

β-aminocampholytic acid

Cal. for C_8H_{14}(COOH)(CH_2NH_2): 185

.318	22.1	.133	199
.389	21.8	.167	197

Isodihydroaminocampholytic acid

Cal. for C_8H_{14}(COOH)(NH_2): 171

1.0151	22.177	.439	192
1.2741	17.877	.692	190

The above results were obtained by the powdered ice equilibrium method. They probably cannot be regarded as being accurate to more than 1 to 2 percent.

It is obvious that at the dilutions used that the addition of one molecule of water to the amino group would have practically no effect on the concentration and hence no effect on the molecular weight. For example if one molecule of water were added to the isodihydroaminocampholytic acid in the above molecular weight determination, this amount of water would be only about .1 gram and hence no appreciable effect would be observed.

How, then, are we to account for the high results obtained in the case of all the acids except aminocamphonanic

acid? The only way that it is possible to logically do this is to assume that association has taken place. And if association has taken place the acidic and basic constants must be greater than 10^{-9}. If these constants were 10^{-8}, assuming complete ionization the degree of hydrolysis would be .92 and hence the remainder of the molecules might be in the form of double molecules. It is possible that the slight degree of polarization of the inner salt of amino camphonanic acid is the cause of its acidic and basic constants being very much smaller than those of the other acids. These constants can be determined by determining the degree of hydrolysis of the hydrochlorides and sodium salts.

As has been shown above, the inner salt structure for amino camphonanic can only be due to its having a very small degree of polarization. Just why it should have a low degree of polarization while the other acids have a higher degree cannot be definitely stated. With the exception of the isodihydroaminocampholytic acid, all the acids, according to all chemical actions show themselves to be cis compounds, so that on the face of it, with the above exception, all should be only slightly polarized if any one is slightly polarized. The difference, as far as we can say lies in some internal structure of the molecule or atom concerning which we are not familiar.

It is not meant to be implied that a solution of aminocamphonanic acid exists entirely as the inner salt

structure, or that the other acids contain none of the inner salt. Probably the best we can say is that in the case of the solution of aminocamphonanic acid 90 percent exists as inner salt, while in the case of the other acids less than 10 percent is in the form of the inner salt.

In conclusion it is hardly necessary to state that the problem is at best only in a qualitative state. The acidic and basic constants of the acids must be determined and the effect of dilution upon the rotation and hydrolysis must be determined.

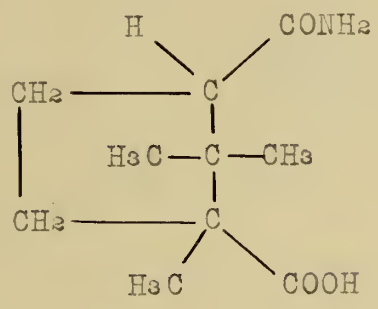
2. NO INVERSION IN THE PREPARATION OF AMINOCAMPHONANIC ACID FROM α-CAMPHORAMIDIC ACID.

As has been stated in Part I of this paper Hoogewerf and Van Dorp[1] reported a melting point of 260° for their aminocamphonanic acid. In Part III of this paper it is shown that by varying the method of preparation it was not possible to obtain an acid with a melting point of 260°. In all cases an acid was obtained which, in a capillary tube showed no signs of melting at any temperature and sublimed above 300°. Professor Bredt in a conversation with Professor Noyes suggested that perhaps there was more than one amino acid formed during the treatment of α-camphoramidic acid with sodium hypobromite. Such a possibility seemed rather remote but it was deemed advisable to make an attempt to isolate a second product. There seemed to be about as much possibility of an inversion or partial inversion taking place during the preparation of the free acid from the hydrochloride as during the preparation of the hydrochloride from the α-camphoramidic acid. Hence this method, as shown in Part III was varied but with the same results, namely that only one acid, and that an acid with no melting point, was obtained.

---

1. Am. 16, 506 (1894)

Since the α-camphoramidic acid is prepared directly from d-camphoric acid anhydride there seems to be no doubt but that α-camphoramidic acid is a cis compound, that is, its formula is



If the hydrogen and amide group had been inverted the compound would have been α-isocamphoramidic acid, a derivative of l-isocamphoric acid. This acid has never been prepared, but its methyl ester was prepared by Noyes and Littleton[1] and its melting point is 126° - 127°. The methyl ester of α-camphoramidic acid was prepared by Van der Meulen[2] through the α-isoimide and it has a melting point of 152°-153°. If the methyl and carboxyl groups had been inverted a derivative of d-isocamphoric acid would have been obtained. If the groups on both the secondary and tertiary carbons had been inverted a derivative of l-camphoric acid would have been obtained. But if any of the above inversions had taken place at least some of the normal product would have been

---

1. J. Am. Ch. Soc. 35, 78 (1913)

2. Rec. trav. chim. 15, 323 (1896)

obtained, and since only one α-camphoramidic acid has ever been isolated we may be sure that this acid is the cis acid.

We will now consider the transformation of α-camphoramidic acid into aminocamphonanic acid hydrochloride. If any inversion at all would take place during the Hoffmann reaction, in this case the transformation would be on the secondary carbon and the product would be isoaminocamphonanic acid hydrochloride. This latter acid has been obtained[1] from the methyl ester of α-isocamphoramidic acid, and it has a melting point of 320°, while the hydrochloride obtained from the α-camphoramidic acid melts at 303° - 305°. Possibly the strongest proof that the latter hydrochloride is a cis compound is that, as shown in Part III of this paper, upon treatment with sodium acetate and acetic anhydride a theoretical yield of an anhydride is given and this anhydride has the normal molecular weight. And also, if an inversion had taken place it is inconceivable that it would have been complete and only one compound formed. And it is shown in Part III that only one compound is formed.

It is quite inconceivable that an inversion could take place in changing from the hydrochloride to the free acid. But as above stated this possibility was considered

---

1. Noyes and Littleton, J. Am. Ch. Soc. 35, 80 (1913)

but only the one free acid was isolated and this is undoubtedly the cis acid for both the free acid and the hydrochloride give practically theoretical yields of a monomolecular anhydride.

How, then are we to account for the anomolous results in the melting point determination? The only possibility that seems to be open is that Hoogewerf and Van Dorp's sample was perhaps not quite dry when a melting point was taken. A melting point determination of a sample not quite dry was taken by the writer and between 260° and 270° the material apparently melted. But the same sample, when carefully dried showed no signs of melting at any temperature.

PART III.

EXPERIMENTAL.

PART III.

EXPERIMENTAL.

Camphoric Acid. The camphoric acid was prepared according to the method given in W. A. Noyes Organic Chemistry for the Laboratory, 2nd edition, page 122. The nitric acid was used for the oxidation of four lots of camphor. The average yield was 800 grams of the crude acid from 1000 grams of camphor.

Camphoric Anhydride. With some modifications the method as given by Noyes[1] was used. 250 grams of the dry crude camphoric acid was placed in a 700 c.c. flask and 150 c.c. of acetic anhydride and 25 c.c. of acetyl chloride were added. A small watch glass was placed over the mouth of the flask. The flask was first heated on the water-bath until the camphoric acid had partly gone into solution. It was then gently boiled for one-half hour over a small Bunsen burner. The hot clear contents of the flask were poured into a porcelain dish and 50 c.c. of water added. After cooling the camphoric anhydride was sucked off thoroughly on a Buchner funnel. It was then washed with 50 percent alcohol. The yield obtained by this method varied from 195 to 210 grams of the crude anhydride.

α-and β-camphoramidic acids. For the preparation of these acids the method of Noyes and Taveau,[2]

---

1. Am. Ch. J. 16, 506 (1894)
2. Am. Ch. J. 32, 287 (1904)

with considerable modification was used. 100 grams of the crude camphoric anhydride was placed in a 350 c.c. magnesium citrate pressure bottle and 125 c.c. of ammonia (0.90) was added and the stopper immediately clamped down. It was allowed to heat up spontaneously until the maximum temperature (65° - 70°) had been reached. The bottle was then placed on the water bath and heated until a clear solution was given. This usually took about ten minutes. It is probably not an unwise precaution to wear goggles and keep the bottles covered with a towel during the heating, but the writer never has had an explosion. After the material has all gone into solution the bottle is removed from the water bath and the stopper very carefully removed before the solution has cooled. The solution is then poured into a beaker and quickly but thoroughly cooled. The now almost solid material is very completely sucked off in a Buchner funnel. The pump is stopped and the ammonium salt is moistened with a little water and again sucked off. The material in the funnel, which is mainly the ammonium salt of the α-camphoramidic acid, is dissolved in about its own weight of hot water and then allowed to cool. After filtration the now quite pure ammonium salt is dissolved in about five times its own weight of cold water, filtered, and to the solution dilute hydrochloric acid is added drop by drop and with constant stirring until a green reaction is given with methyl violet paper. The α-camphoramidic acid is filtered off and allowed to dry in the air. In all

cases an acid melting no lower than 175° and no higher than 177 was given. The melting point[1] of the pure acid is 176°-177°. The mother liquors from the recrystalization of the ammonium salt may be used for the recrystalation of a second and third lot of the acid salt. To the other liquors from the filtration of the crude ammonium salt one mol. (67 c.c.) of sodium hydroxide solution (3 c.c. = 1 gram) were added. After a few minutes a copious precipitate of the sodium salt of the β-camphoramidic acid is given. This is filtered, washed, recrystallized and the free acid obtained in the same manner as given above for the acid. In all cases an acid is given with a melting point between 180° and 183°. The pure acid[2] melts at 182° - 183°. The motherliquors from the recrystallization of the sodium salt may be used for a second and third lot of the salt. Then the mother liquors from the recrystallization of this third lot together with the mother liquors from the recrystallization of the ammonium salt are added to the filtrate from the filtration of the crude sodium salt of the β-acid. To this solution concentrated commercial hydrochloric acid is very slowly added until a green reaction is given with methyl violet paper. Unless great care is exercised the mixture of the camphoramidic acids will be precipitated as a gummy mass. Under the best of conditions

---

1. Hoogewerf and Van Dorp. Rec. trav. chim. 14, 260 (1895)
2. Noyes. Am. Ch. J. 16, 310 (1894)

there is always some amorphous material formed, but this will become crystalline upon standing in contact with the solution for several hours. The mixed acids are then filtered and dried. The proceedure with these mixed acids is just the same as with the camphoric anhydride except that it is not necessary to use the pressure bottles. Working quite carefully, from a lot of 200 grams of the anhydride 120 grams of the α-acid and 65 grams of the β-acid was obtained.

Aminocamphonanic acid hydrochloride. 25.5 c.c. (1 mol) of bromine was aspirated through 700 c.c. of 10 percent sodium hydroxide and this solution was added to a solution of 100 grams (1/2 mol) of α-camphoramidic acid in 500 c.c. of 10 percent sodium hydroxide. This mixture was heated for one half hour at 70° to 80°. Sodium sulphite was then added until a little of the solution shows no bromine color upon acidification with hydrochloric acid. After cooling the solution is carefully poured into a large flask containing 200 c.c. of concentrated (1.19) hydrochloric acid. This is slightly in excess of the amount of acid necessary to give the hydrochloride of the amino acid. The solution is evaporated on the water bath until crystals start to form. It is then cooled and the aminocamphonanic acid hydrochloride, together with a small amount of sodium chloride, is filtered off. The filtrate is evaporated to dryness and the residue ground up in a mortar with 95 percent alcohol. The alcohol solution, which contains the remainder

of the hydrochloride of the acid is diluted with about one-half its volume of water and evaporated to dryness and the residue added to the acid hydrochloride obtained above.

It is permissable to proceed with the preparation of the free acid from this crude hydrochloride. Some of it, however, was very carefully purified by recrystallization from hot water. It was found necessary to filter the hot solution through animal charcoal in order to free it from a persistent brown coloration. After three recrystallizations it gave a melting point of 304° - 305°. Noyes[1] gives the melting point as 303° - 305°. $(\alpha)_D^{24^\circ} = 25.0^\circ$, 1.0 gram in 10 c.c. of water solution.[2]

An attempt to isolate a second aminocamphonanic acid hydrochloride. The possibility of there being more than one aminocamphonanic acid hydrochloride has been discussed in Part III of this paper. It is obvious since a pure salt, as indicated by the constancy of the melting point and specific rotation, was obtained by the procedure given for the preparation of the hydrochloride that a second salt, if it exists, must be more soluble than the one obtained above. Therefore starting with 200 grams of α-camphoramidic acid, the procedure as outlined above was followed until the alcoholic

---

1. Am. 16, 507 (1894)
2. All rotations determined by the writer and given in this paper were determined in a one decimeter tube and the specific rotation calculated by the following formula $(\alpha)_D = \frac{100a}{lm}$, where a = observed rotation, l = 1, the length of tube, and m = mass of material in 100 c.c. of solution.

extract was obtained. The residue from the evaporation of this extract was recrystallized twice from water, the mother liquors being saved. The recrystallized product showed a melting point of 303° - 304°, and specific rotation $(\alpha)_D$ = 24.8. Therefore this is the same hydrochloride. The mother liquors obtained from the recrystallization were partially evaporated, then cooled and the salt filtered, there being about 10 c.c. of the filtrate. The salt was recrystallized twice from water and the product showed a melting point of 298° - 310 , the material becoming very brown upon melting. It was thought that the salt contained some of the hydrobromide so it was dissolved in concentrated hydrochloric acid and evaporated to dryness on the water bath. This was repeated three times. The final product was recrystallized twice from hydrochloric acid and a salt was given which showed a melting point of 303° - 305°. Its specific rotation $(\alpha)_D$ = 24.7.

If the second hydrochloride, if present, were insoluble in alcohol it would not have been recovered in the method just given. With this in mind the following modification was used. Starting with 100 grams of α-camphoramidic acid the procedure as outlined above was followed until the point where it was customary to evaporate the mother liquors from the filtration of the first lot of hydrochloride. Instead of evaporating the mother liquors to dryness they were evaporated until a considerable sodium chloride had separated. The mixture was filtered while hot and a quantity of material

separated from the mother liquors upon cooling. This was filtered. Hydrochloric acid was added to the mother liquors of which there were about 40 c.c. and the solution was evaporated to dryness. The residue was dissolved in concentrated hydrochloric acid and the solution evaporated to dryness. This was repeated two more times and the residue after the final evaporation was recrystallized twice from water. Its melting point was 301° - 304°, and its specific rotation $(\alpha)_D = 24.6$. It is therefore the same hydrochloride.

Aminocamphonanic acid. Two methods were used for the preparation of the free acid from the hydrochloride.

First method. 275 grams of crude aminocamphonanic acid hydrochloride was mixed to a thin paste with 275 c.c. of water. To this mixture was added 139 c.c. of sodium hydroxide (3 c.c. = 1 gr) (1 mol.) and the whole was digested on the water bath for one half hour, allowed to cool and the aminocamphonanic acid was filtered and washed once with water. This gave 167 grams of acid which was fairly pure. This is 74 percent of the theoretical yield. By adding hydrochloric acid to the above filtrate, evaporating to dryness and then extracting with alcohol, practically all of the unrecovered aminocamphonanic acid may be recovered as the hydrochloride.

Second method of preparation. 100 grams of the crude hydrochloride were dissolved in water and sufficient sodium hydroxide was added to give a solution neutral to phenolphthalein. This meutral point was found by putting a little of the solution

in a test tube, adding a drop of the indicator, and boiling. The amount of sodium chloride was calculated from the amount of the hydrochloride. For 100 grams of the latter substance the equivalent for sodium chloride is about 28 grams. The solution was evaporated to approximately 100 c.c. and the free amino acid is filtered off. 72 grams were given which is 82 percent of the theory. As above the remainder of the acid may be recovered as hydrochloride.

Since the acid is as soluble in cold as in hot water it was purified by evaporation of the water solution, filtering off the crystals after the saturated solution had been about one half evaporated. This was repeated once more and the product obtained showed a specific rotation, $(\alpha)_D^{25} = -29.2$; 10 grams in 100 c.c. of solution. The product was recrystallized once more and exactly the same rotation was given. An attempt was made to obtain a melting point, but in all cases the acid sublimed above 300°. As stated in Part I of this paper Hoogewerf and Van Dorp[1] found a melting point of 260° for this acid. A discussion of the possibility of there being more than one aminocamphonanic acid may be found in Part II of this paper. Below is described an attempt to isolate a form other than the one described above.

Attempt to isolate a second aminocamphonanic acid.

50 grams of quite pure aminocamphonanic acid hydrochloride

---

1. Am. 16, 506 (1894) foot note.

were ground up to a fine powder in a mortar. To the powder 50 c.c. of water, together with the theoretical quantity of sodium hydroxide solution. (29 c.c. of solution. 3 c.c. = 1 gr.) This mixture was shaken vigorously for five minutes and then filtered and the acid washed twice with water. It is then recrystallized twice as above and the specific rotation taken. $(\alpha)_D^{24} = -29.0$. The mother liquors from the filtration of the crude acid are allowed to partially evaporate at room temperature and the crystals formed were collected, washed once with water and recrystallized by dissolving in cold water and allowing the saturated solution to evaporate in the air to about one half the original volume. This was repeated once more. An acid was obtained which was in all respects identical to the ordinary amino camphonanic acid. Hence it is proved beyond a reasonable doubt that only one amino acid is obtained from the α-comphoramidic acid.

For taking the molecular weight some of the acid was recrystallized from water two more times than was necessary to remove all traces of chlorine. Altogether six recrystallizations were necessary.

For taking the molecular weight the same method was used for all the molecular weight determinations given in this paper. The method was as follows: Ice made from distilled water was crushed in a mortar until there were no pieces larger than a pea. It was then put into Dewar bulb

all liquid being kept out of the glass tube by keeping the stop-cock closed. The mixture is stirred and the thermometer lightly tapped until a constant reading is obtained. About 20 c.c. of the liquid is then drawn off through the glass tube. This liquid is weighed in a previously weighed evaporating dish and the solution is then evaporated on the water bath to constant weight. The molecular weight is calculated from the following formula,

$$\text{Molecular weight} = K \frac{(100)\,(\text{Weight of substance})}{(\text{Weight of Water})\,(\text{Freezing point lowering})}$$

$$K = 18.4$$

Aminocamphonanic Acid Anhydride. This substance which was used by the writer in some work, the results of which have already been published,[1] was until the present year prepared in this laboratory either by heating the free aminocamphonanic acid in a retort or by heating the hydrochloride with lime. By these methods a yield of 75 to 85 percent of a quite impure anhydride was obtained. The following method of procedure was found to give practically theoretical yields of a quite pure anhydride. 10 grams of aminocamphonanic acid hydrochloride, 6 grams (1.5 mol.) of fused sodium acetate and 20 c.c. of acetic anhydride were gently boiled in a long necked flask for about 10 minutes. The mixture was allowed to cool somewhat and about a

---

1. Noyes, Gorsline and Potter. J. Am. Ch. Soc. 34, 62 (1912)

10 percent excess of strong sodium hydroxide solution was added. A liquid layer was formed on the top of the alkaline solution. The alkaline solution was heated on the water bath until the liquid layer had changed to a solid substance. This took about five hours. After allowing the mixture to cool it was extracted twice with ether. The ether solution was dried with anhydrous sodium sulphate, and the ether was then distilled off from a bulb which had been previously weighed. 7.3 grams of pure white anhydride was given. This practically is a 100 percent yield. This percentage yield was repeatedly duplicated. Recrystallizing the product once from petroleum ether gave a product melting at 200° - 203°. A second recrystallization gave a product melting quite sharply at 203°. A third recrystallization did not raise the melting point. This corresponds to what had been previously found.[1] $(\alpha)_D^{29°} = -60.5$; 1 gr. in 10 c.c. of absolute alcohol solution. $(\alpha)_D^{28} = -60.6$; .5 gr. in 10 c.c. water solution. Noyes and Taveau[2] found $(\alpha)_D^{26} = -60.1$ for a 10 percent alcohol solution.

A molecular weight determination was made of a sample which was purified by recrystallizing two more times than was required to give a melting point of 203°

---

1. Noyes. Am. 16, 507.

2. Am. 32, 288.

Gr. Substance	Gr. Water.	Δt_F	M.W.	Cal. for $C_8H_{14}{}^{NH}_{CO}$
.373	20.9	.208	157	153
.750	20.1	.432	159	

Hydrolysis of Aminocamphonanic Acid Anhydride.

.5 gram of the anhydride was roughly weighed out and placed in a tube and water was added to give 10 c.c. of solution. A few c.c. were taken from the tube and a rotation taken. $(\alpha)_D$ = -59.8. The tube was sealed and heated on the water bath for three days. After removal and cooling the rotation was again taken and it was found to be unchanged. Hence no hydrolysis had taken place. To this solution was then added 5 c.c. of sodium hydroxide (3 c.c. = 1 gr.). A flocculent white precipitate forms. This mixture was heated for three days on the water bath and allowed to cool. The same precipitate is present. This is filtered and recrystallized once from petroleum ether. Its melting point was found to be 200° - 203°. Mixed with pure anhydride the melting point was unchanged.

3 grams of the anhydride are heated on the water bath with 20 c.c. of 1 - 1 hydrochloric acid for 10 hours. The solution was then evaporated to about one-third its original volume, allowed to cool and the needle-like crystals filtered off. The crystals were dissolved in the minimum amount of water and a few c.c. of concentrated hydrochloric

acid added. The precipitate which is formed is filtered, washed once with water, dried, and a rotation taken. $(\alpha)_D^{24} = 24.9$. Therefore the anhydride is hydrolysed back to the hydrochloride of aminocamphonanic acid.

Acetyl Derivative of Aminocamphonanic Acid Anhydride.

It will be remembered that in the description of the method for the preparation of aminocamphonanic acid anhydride by treating the acid hydrochloride with acetic anhydride and sodium acetate that after boiling the solution and then adding sodium hydroxide, a liquid layer was left on top. It was decided to investigate this product. 6 grams amino-camphonanic acid hydrochloride, 3.5 grams sodium acetate and 12 c.c. of acetic anhydride were boiled together for 10 minutes. After cooling not quite enough sodium hydroxide solution was added to neutralize the acetic acid and anhydride. The mixture was then extracted with petroleum ether three times and the petroleum ether there washed three times with water. After drying with sodium sulphate the ether was distilled off and 4 - 5 grams of a slightly yellow liquid was given. This was distilled. About 10 percent of the liquid came off below 260°, 80 percent between 260° - 262° and the remainder between 262° - 270°. There was slight decomposition of the last fraction. $(\alpha)_D = +72.7$; 0.544 gr. in 5 c.c. of alcohol solution. One gram when heated for a few hours with 10 percent sodium hydroxide solution was changed to a solid which after

recrystallization from petroleum ether gave a melting point of 201° - 203°. Some of the crystals, when mixed with pure aminocamphonanic acid anhydride, showed the same melting point. Some of the liquid when shaken with dilute hydrochloric acid gave no precipitate with sodium nitrite solution. From these facts it was concluded that we had the acetyl derivative of aminocamphonanic acid anhydride.

Analysis:

Calculated for $C_8H_{14}\begin{matrix}NC_2H_3O\\ |\\ CO\end{matrix}$ N 7.16

Found N 7.05

Nitroso Derivative of Aminocamphonanic Acid Anhydride. Since the rotation of this compound has never been taken it was thought desirable to prepare it and take its rotation. It was prepared in just the same manner that Bredt[1] originally prepared it. About one gram of the aminocamphonanic acid anhydride was dissolved in 10 c.c. of dilute hydrochloric acid (1 - 4) and .5 gram of sodium nitrite in solution was added. A yellow oil first separates and this soon turns to a crystalline mass. It was filtered and recrystallized twice from hot alcohol. The yellow needles obtained showed a melting point of 138° - 139°. A third recrystallization gave a product

---

1. Ber. 35, 1291 (1902).

melting at the same temperature. $(\alpha)_D^{24} = 153$; 0.25 gr. in 10 c.c. of alcohol solution.

Cyanocamphonanic Acid. Proceeding with the preparation of this acid according to the method of Hoogewerf and Van Dorp,[1] there was obtained about the same yield of crude acid which they obtained, namely about 50 percent. It was thought, since the hydrochloride of the α-isoimide obtained by treating the α-camphoramidic acid with acetyl chloride is very easily hydrolysed by water to the α-camphoramidic acid, that perhaps by suspending the isoimide hydrochloride in petroleum ether and passing in dry ammonia gas that the yield could be increased. The following procedure was used. 12.5 grams of α-camphoramidic acid and 50 grams of acetyl chloride were placed in a flask which was attached to a reflux condenser. The flask was heated on the water bath. A solution is first formed and in about two minutes the contents of flask apparently become solid. The flask and material is then cooled, the material filtered and the solid washed with carbon disulphide. Up to this point the method of procedure has been just the same as given by the above mentioned investigators. Instead of adding the isoimide hydrochloride to 12 percent ammonia as they did, it was shaken with petroleum ether and a slow stream of dry ammonia

---

1. Rec. trav. chim. 14, 261 (1895)

gas was passed through the mixture until saturation was reached. Dilute ammonia was added to dissolve the ammonium salts and from the aqueous solution the cyanoacid was precipitated with dilute hydrochloric acid. The hydrochloric acid solution must be added drop by drop or the cyano acid will be precipitated as a gummy mass. The crystalline acid was filtered and, after drying, was weighed. 10 grams or 84 percent of the theor, was given. For purification two methods were used, one by recrystallization from hot water, which was the method used by Hoogewerf and Van Dorp, and the other consisted of dissolving the acid in ammonium hydroxide and precipitation with hydrochloric acid. Recrystallization from hot water. 5 grams of the crude acid, whose melting point was about 130° - 140°, was dissolved in the minimum amount of boiling water and the solution was allowed to cool slowly. After the solution was cold it was filtered and a portion of the acid was dried and a melting point taken. It showed a melting point of 143° - 148°. Proceeding again as above a melting point of 148° - 150° was given. The third time a product melting at 150° - 151° was given. This is the melting point given by Hoogewerf and Van Dorp[1]. A small portion of the product was recrystallized a fourth time and the same melting point was given. After drying and weighing it was found that 2.4 grams of the pure acid were given.

---

1. Rec. trav. chim. 14, 261 (1895).

Purification by dissolving in dilute ammonia and precipitation with hydrochloric acid. 5 grams of the crude acid (130° - 140°) were dissolved in the minimum amount of 8 percent ammonia and the acid was very carefully precipitated with hydrochloric acid. The mixture was filtered and a portion of the crystals were dried and they showed a melting point of 145° - 149°. The same procedure was repeated and a product melting at 149° - 151° was given. For all practical purposes this is sufficiently pure, but for purposes of comparison the operation was gone through once more. This time 3.1 grams of an acid melting at 150° - 151° was given. $(\alpha)_D^{26}$ = 67.3; 1 gr. in 10 c.c. of alcohol solution. Hoogewerf and Van Dorp[1] give exactly the same for a 6 percent alcoholic solution.

α-aminocampholic acid hydrochloride. The only variation from the method of preparation of Hoogewerf and VanDorp[1] or Rupe and Splittgerber[2] was that a somewhat larger portion of sodium was used in the reduction. 5 grams of cyanocamphonanic acid were dissolved in 50 c.c. of absolute alcohol and 15 grams of sodium were added in small portions, the flask being connected to a reflux condenser. During the addition of the sodium about 20 c.c. more of alcohol were added. After all the sodium had dissolved water was added and the solution was evaporated until the odor of alcohol was no

---

1. Rec. trav. chim. 14, 261 (1895).

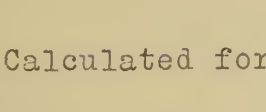
2. Ber. 40, 4313 (1907).

longer given. From this point on an entirely different method of separation and purification of the hydrochloride was used than was used by Rupe and Splittberger.[1] Hydrochloric acid in slight excess was added to the cold solution and it was then extracted three times with ether in order to remove any unchanged cyano-acid. Upon evaporation of the ether solution it was found that about one gram of cyano acid was given. This was used in subsequent reductions. The hydrochloric acid solution was evaporated to dryness and the residue ground up in a mortar with alcohol. The alcohol was filtered, diluted, with water and the alcohol was evaporated. The brown turbidity of the solution was then removed by filtering twice through powdered animal charcoal. The clear solution was then evaporated on the water bath until crystals started to form, when it was removed and allowed to cool and filtered. The very slightly brown crystals were dissolved in the minimum amount of hot water, filtered again through aminal charcoal and after cooling the pure white needle like crystals were filtered, dried and a melting point taken. It was found to be 248° - 250°. A portion was again recrystallized and the same melting point was given. Rupe and Splittgerber[1] give the melting point as 247° - 248°. The specific rotation which had never been taken before, was obtained $(\alpha)_D^{24°} = 44.7$; 0.5 gr. in 10 c.c. of water solution. It

---

1. Ber. 40, 4313 (1907).

was analysed for chlorine,

Calculated for C_8H_{14} 		Cl	16.00
	Found	Cl	16.17

α-aminocampholic acid. An attempt was made to prepare the free acid from its hydrochloride in the same manner that aminocamphonanic acid is prepared from its hydrochloride, but the free acid was apparently more soluble than sodium chloride so this method was abandoned. Instead the hydrochloride was dissolved in water and sodium hydroxide added until an outside test with phenolphthalein showed a very faint alkaline reaction. The solution after filtering was evaporated to dryness and ground up in a mortar with alcohol, the alcohol filtered, diluted and partially evaporated. The slightly turbid solution was filtered through charcoal and then the solution was evaporated until only a few c.c. of liquid was left, a large mass of crystals having separated during the evaporation. The crystals were filtered off and recrystallized by evaporation of the water solution, the acid being practically as soluble in cold as in hot water. This was repeated three times more and then showed no trace of chlorine. The molecular weight was determined with this sample. Heated in a capillary tube no melting point was obtained but considerable decomposition took place between 300° and 320°, depending upon the rate of

heating. $(\alpha)_D^{26} = 67.0$; .207 gr. in 10 c.c. of solution.

α-camphidon. This was prepared from the hydrochloride of α-aminocampholic acid in precisely the same manner as the anhydride of aminocamphanic acid was prepared from the hydrochloride of aminocamphonic acid. After making the acetic anhydride solution alkaline with sodium hydroxide the same liquid layer was observed on the surface that was observed in the preparation of the above mentioned anhydride. This was very likely the aceytl derivative but no attempt was made to isolate it. Practically a theoretical yield of the anhydride was given which melted at 229° - 231°. Recrystallizing once from petroleum ether a product melting at 230° - 231° was given. $(\alpha)_D^{25} = -33.9$; 0.5 gr. in 10 c.c. alcohol solution. Rupe and Splittgerber[1] give $(\alpha)_D = -37.2°$ in 10 percent benzol solution.

Analysis,

Calculated for $C_8H_{14}\begin{matrix}CH_2\\CO\end{matrix}>NH$ N 8.38

Found N 8.42

Nitroso derivative of α-camphidon. The α-camphidon was dissolved in hydrochloric acid (1 - 4) and sodium nitrite solution slowly added. The yellow crystals

---

1. Ber. 40, 4313 (1907).

formed were filtered, dried and recrystallized from hot alcohol. The lemon-yellow needle-like crystals gave a melting point of 125° - 126°. The product given by a second recrystallization showed the same melting point. $(\alpha)_D^{23} = -59.0$; 0.25 gr. in 10 c.c. alcohol. From analogy to the well known nitroso derivatives of aminocamphonanic and dihydroaminocampholytic acid anhydrides it was not thought necessary to analyse the compound for identification.

Aminodihydrocampholytic acid. This acid was prepared in the same manner as described by Noyes[1] except that a more elaborate method was followed in recovering the last traces of the acid. The procedure followed was identical to that for the preparation of aminocamphonanic acid from α-camphoramidic acid, except that β-camphoramidic acid was used and instead of adding sufficient hydrochloric acid to give the acid hydrochloride, only enough was added to give a solution exactly neutral to phenolphthalein. After this point the solution was evaporated until it was thought the sodium chloride was starting to come down. The crystals of the amino acid were then filtered and to the filtrate an excess of hydrochloric acid was added and the whole evaporated to dryness, and the residue extracted with alcohol. Since the dihydroaminocampholytic acid is quite easily esterified the alcoholic solution was diluted

---

1. Am. 16, 503 (1894).

with considerable water and just enough sodium hydroxide solution added to give a solution neutral to phenolphthalein. It was then partially evaporated and the amino acid filtered off. An excess of hydrochloric acid was added to this filtrate and the same procedure followed as above. Since the acid is no more soluble in hot than in cold water and is not soluble in any other solvent it must be purified by dissolving in water and partial evaporation. For ordinary purposes one recrystallization is sufficient. For taking the molecular weight and rotations an acid was used which had been recrystallized six times, two more times than was necessary to free it from traces of chlorine. The results on the molecular weight determinations are given in Part II of this paper. $(\alpha)_D^{25} = 54.7$; 0.5 gr. in 10 c.c. of water solution. Noyes and Phillips[1] give $(\alpha)_D = 53.7$ for the saturated solution. (about 7.5 percent).

Dihydroaminocampholytic acid hydrochloride. A few grams of the free acid were shaken with a few c.c. of water and sufficient hydrochloric acid was added to give a green color to methyl violet paper. The solution was then partially evaporated and upon allowing to cool the hydrochloride separates. It was filtered and recrystallized from hot water again. A melting point of 262° - 263° was given. Recrystallizing again

---

1. Am. 24, 290 (1900).

gave a product melting at 261° - 262° which is the same as that reported by Noyes.[1] $(\alpha)_D^{26} = 41.3$; 1 gr. in 10 c.c. of water solution.

Dihydroaminocampholytic acid anhydride. This substance was prepared either by treating the free acid with acetic anhydride or by treating the hydrochloride of the acid with sodium acetate and acetic anhydride and subsequently heating the mixture with an excess of sodium hydroxide. In the latter method it is probable that the acetyl derivative is formed as the similar liquid layer was always formed on addition of the excess of sodium hydroxide to the acetic anhydride solution. The latter method of preparation has the advantage of allowing quite impure hydrochloride to be used. The melting point, 188° - 189°, and the specific rotation, $(\alpha)_D^{30} = 72.8$, have already been published.[2]

Nitroso derivative of dihydroaminocampholytic acid anhydride. Since the rotation of this substance had never been obtained it was thought desirable to obtain it. It was prepared according to a method previously reported.[2] $(\alpha)_D^{24} = 83.3$; 0.25 gr. in 10 c.c. of absolute alcohol solution.

Dihydrocyanocampholytic acid. Hoogewerf and Van Dorp[3] prepared this acid in just the same manner that they prepared

---

1. Am. 16, 504 (1894).
2. Noyes and Potter. J. Am. Ch. Soc. 34, 1072 (1912).
3. Rec. trav. chim. 14, 267 (1895).

the cyanocamphonanic acid. Rupe and Splittgerber[1] proceeded in essentially the same manner. Starting with 12.5 grams of β-camphoramidic acid and proceeding in precisely the same manner as in the preparation of the cyanocamphonanic acid 9.5 grams of crude acid was obtained which is an 80 percent yield. There was not nearly as much tendency to form a gummy precipitate as was noted in the case of the cyanocamphonanic acid. The crude acid was purified by dissolving in 8 percent ammonia and precipitating with hydrochloric acid. One such proceedure sufficed to bring the melting point up to 109° - 110°. A portion was recrystallized again in the same manner but no change in the melting point was observed. The above is the melting point observed by Hoogewerf and Van Dorp.[2] $(\alpha)_D^{22} = 25.3$ 0.6 gr. in 10 c.c. of alcohol solution. Hoogewerf and Van Dorp[2] give the specific rotation $(\alpha)_D = 18.12$ for a 6 percent alcohol solution. Since they purified their acid by recrystallization from hot water, in order to clear up the remote possibility of this causing the difference in the rotation, some of the crude acid was purified by their method, but a rotation taken after the fourth recrystallization, gave a value $(\alpha)_D = 25.2$ and after the fifth recrystallization $(\alpha)_D = 25.3$ so there is little doubt but that this is the correct value.

---

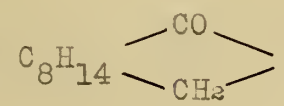
1. Ber. 40, 4313 (1900).

2. Rec. trav. chim. 14, 267 (1895).

β-aminocampholic acid hydrochloride. Starting with dihydrocyanocampholytic acid the procedure for the preparation, separation, and purification of this substance was the same as the preparation of the α-aminocampholic acid hydrochloride. It was found, however, that the reduction in the case in hand was not as complete as with the cyano-camphonanic acid. It was found more advisable to simply separate the unchanged cyano acid by extraction of the acid solution with ether than to use more sodium and alcohol. The β-aminocampholic acid hydrochloride is somewhat less soluble than its isomer and hence it is more easily purified. After two recrystallizations its melting point was 218° - 220°. $(\alpha)_D^{26}$ = 41.3; 0.5 gr. in 10 c.c. of water solution.

β-aminocampholic acid. About 5 grams of the pure hydrochloride were dissolved in the minimum amount of water and sufficient strong sodium hydroxide solution (3 c.c. = 1 gr) was added to give a solution neutral to phenolphthalein. The free acid, which was precipitated was filtered, dissolved in hot water, partially evaporated and filtered. This was repeated until a substance free from chlorine was obtained, three recrystallizations in all being required. $(\alpha)_D^{25}$ = 16.4; 0.25 gr. in 10 c.c. of solution. The molecular weight determinations are given in Part II of this paper.

β-camphidon. This compound was prepared from the β-aminocampholic acid hydrochloride in just the same manner as the α-camphidon is prepared from the α-aminocampholic acid. A melting point of 234° - 235° was found and a specific rotation $(\alpha)_D^{24} = 63.2$; 0.25 gr. in 5 c.c. of alcohol solution. Rupe and Splittgerber[1] report a melting point of 225° and its specific rotation $(\alpha)_D = 66.5$ for a 10 percent benzol solution. An analysis of the compound was made.

Calculated for C_8H_{14}  N 8.38

Found N 8.37

Nitroso derivative of β-camphidon. The α-camphidon was dissolved in dilute hydrochloric acid (1 - 4) and sodium nitrite solution was added. The yellow precipitate was filtered and recrystallized from alcohol two times, when a melting point of 164° - 165° is given. A portion recrystallized a third time showed the same melting point. $(\alpha)_D^{23} = 103$; 0.25 gr. in 10 c.c. of solution.

---

1. Ber. 40, 4313 (1907).

B I O G R A P H I C A L.

BIOGRAPHICAL.

The writer received his early education in the schools of Fairbury, Illinois, graduating from the high school at that place in 1906. The following fall he entered Lake Forest College, taking the degree of Bachelor of Arts in 1909, the major work being in Chemistry and Physics. In the fall of 1909 he entered the Graduate School of the University of Illinois and received the degree of Master of Science in 1911 from the same place. During the collegiate year 1909 - 1911, he was Graduate Assistant in Chemistry. Since January 1st, 1911 he has held the position of Research Assistant to Professor W. A. Noyes.

He has published the following papers:

"Camphonolic Acid and Camphonololactone" with Dr. W. A. Noyes and Dr. E. E. Gorsline.

"Campholytic Acid and Related Compounds. Walden's Rearrangements". with Dr. W. A. Noyes.

He is a member of Gamma Alpha Scientific Fraternity, Alpha Chi Sigma and Phi Lambda Upsilon. He is also a member of the American Chemical Society and has just accepted an invitation to join Sigma Xi.

UNIVERSITY OF ILLINOIS-URBANA
3 0112 086829436